ENGOT-en7/MaNGO/AtTEnd

Phase III double-blind randomized trial of atezolizumab in combination with paclitaxel and carboplatin in women with advanced/recurrent endometrial cancer

Atezolizumab Trial in Endometrial cancer

Last update, June 25th 2020

GENERAL INFORMATIONS

Principal Investigator: Nicoletta Colombo, European Insitute of Oncology (IEO) - Milan

Sponsor: Mario Negri Gynecologic Oncology (MaNGO) - Milan

Supporters: F. Hoffmann-La Roche Ltd, Chugai Pharmaceutical Co. Ltd

Involved countries: Italy, Austria, Australia, Germany, Japan, New Zealand, Spain, Switzerland, UK

No. of involved sites: about 94

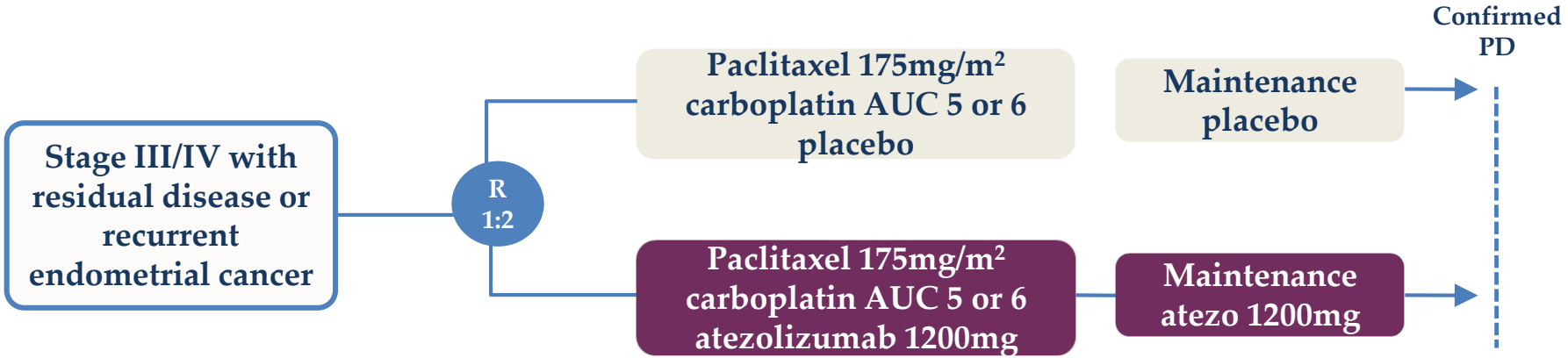
Study duration: 2 years accrual - 2 years follow-up

Status: Recruiting (First Patient In: 3rd October 2018)

Planned No. of patients: 550

STUDY DESIGN

PHASE III, RANDOMIZED, DOUBLE-BLIND



550 patients stratified by:

- Country of the experimental center
- Histological type (endometrioid vs. other types)
- Disease (recurrent disease vs advanced disease at primary diagnosis)
- MS status (MSS vs MSI vs non-evaluable)

INCLUSION CRITERIA

I-1.Newly diagnosed, histologically-confirmed with residual disease after surgery either measurable or evaluable, or inoperable stage III-IV endometrial carcinoma/carcinosarcoma after diagnostic biopsy, and naïve to first line systemic anti-cancer treatment. Recurrent endometrial cancer patients if not yet treated for recurrent disease.

(Presence of residual disease is mandatory for newly diagnosed cases who underwent primary surgery)

I-2. Eastern Cooperative Oncology Group (ECOG) performance status 0-2

I-3. Age ≥ 18 years

I-4.In recurrent patients, only one prior line of systemic platinum-based regimen is permitted if the platinum-free interval ≥ 6 months.

I-**5**.Patients with history of primary breast cancer may be eligible provided they completed their definitive anticancer treatment more than 3 years ago and they remain breast cancer disease free prior to start of study treatment.

I-6.Previous pelvic and outside pelvis radiation is allowed, except for whole abdominal radiotherapy, if completed more than 6 weeks ago.

I-7. Signed informed consent and ability to comply with treatment and follow-up.

I-8.Representative FFPE tumor sample or, only if unfeasible, at least 20 unstained slides from initial surgery or from diagnostic biopsy, in case surgery was not performed, available and sent to central laboratory for MS determination prior to randomization.

I-9. Patients must have normal organ and bone marrow function

EXCLUSION CRITERIA (I)

E-1. Other malignancy within the last 5 years except: adequately treated non-melanoma skin cancer, curatively treated in situ cancer of the cervix, ductal carcinoma in situ (DCIS) of the breast. Patients with a history of localized malignancy diagnosed over 5 years ago may be eligible provided they completed their adjuvant systemic therapy prior to randomization and that the patient remains free of recurrent or metastatic disease

E-2. Uterine leyomiosarcoma.

E-3. Major surgery within 4 weeks of starting study treatment or patients who have not completely recovered from the effects of any major surgery.

E-4. Previous allogeneic bone marrow transplant or previous solid organ transplantation**.**

E-5. Administration of other simultaneous chemotherapy drugs, any other anticancer therapy or anti-neoplastic hormonal therapy, or simultaneous radiotherapy during the trial treatment period (hormonal replacement therapy is permitted).

E-6. Prior treatment with CD137 agonists or immune checkpoint blockade therapies, anti–PD1, or anti–PDL1 therapeutic antibodies or anti-CTLA4 .

E-7. Treatment with systemic immunostimulatory agents (including but not limited to interferon-alpha (IFN-α) and interleukin-2 (IL-2)) within 4 weeks or five half-lives of the drug (whichever is shorter) prior to Cycle 1 d1

EXCLUSION CRITERIA (II)

E-8. Treatment with systemic corticosteroids or other systemic immunosuppressive medications (including but not limited to prednisone, dexamethasone, cyclophosphamide, azathioprine, methotrexate, thalidomide, and anti−tumor necrosis factor [TNF] agents) within 2 weeks prior to Cycle 1 d1, or anticipated requirement for systemic immunosuppressive medications during the trial. However, use of inhaled corticosteroids for chronic obstructive pulmonary disease or for asthma is allowed, as well as the use of mineralocorticoids (e.g., fludrocortisones) and low-dose supplemental corticosteroids for adrenocortical insufficiency and for patients with orthostatic hypotension. The use of corticosteroids as premedication for paclitaxel-based regimen is allowed

E-9. History of autoimmune disease, including but not limited to myasthenia gravis, myositis, autoimmune hepatitis, systemic lupus erythematosus, rheumatoid arthritis, inflammatory bowel disease, vascular thrombosis associated with anti-phospholipid syndrome, Wegener's granulomatosis, Sjögren's syndrome, Guillain-Barré syndrome, multiple sclerosis, vasculitis, or glomerulonephritis [please note: patients with a history of autoimmune hypothyroidism on a stable dose of thyroid replacement hormone are eligible; patients with controlled Type 1 diabetes mellitus on a stable insulin regimen are eligible; history of idiopathic pulmonary fibrosis (including pneumonitis), drug-induced pneumonitis, organizing pneumonia (i.e., bronchiolitis obliterans, cryptogenic organizing pneumonia) is permitted]

E-10. Immunocompromised patients, e.g., patients who are known to be serologically positive for human immunodeficiency virus (HIV).

EXCLUSION CRITERIA (III)

E-11. Patients with active hepatitis B (defined as having a positive hepatitis B surface antigen [HBsAg] test at screening) or hepatitis C

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E-12. Active tuberculosis (all patients will have tuberculin [PPD] skin test or Interferon-Gamma Releasing Assay [IGRA] done locally prior to inclusion to study)

E-13. Signs or symptoms of infection within 2 weeks prior to Cycle 1, Day 1

E-14. Administration of a live, attenuated vaccine within 4 weeks prior to Cycle 1, Day 1 or anticipation that such a live attenuated vaccine will be required during the study. Influenza vaccination should be given during influenza season only (example approximately October to March in the Northern Hemisphere). Patients must not receive live, attenuated influenza vaccine.

E-15. Clinically significant (e.g. active) cardiovascular disease, including:

a. Myocardial infarction or unstable angina within ≤ 6 months of randomization,

b. New York Heart Association (NYHA) ≥ grade 2 congestive heart failure (CHF),

c. Poorly controlled cardiac arrhythmia despite medication (rate controlled atrial fibrillation allowed)

d. Peripheral vascular disease grade ≥ 3 (e.g. symptomatic and interfering with activities of daily living [ADL] requiring repair or revision)

E-16. Resting ECG with QTc > 470 msec on 2 or more time points within a 24 hour period or family history of long QT syndrome.

EXCLUSION CRITERIA (IV)

E-17. History or clinical suspicion of brain metastases or spinal cord compression. CT/MRI of the brain is mandatory (within 4 weeks prior to randomization) in case of suspected brain metastases. Spinal MRI is mandatory (within 4 weeks prior to randomization) in case of suspected spinal cord compression.

E-18. History or evidence upon neurological examination of central nervous system (CNS) disease, unless asymptomatic and adequately treated with standard medical therapy.

E-19. Evidence of any other disease, metabolic dysfunction, physical examination finding or laboratory finding giving reasonable suspicion of a disease or condition that contraindicates the use of an investigational drug or puts the patient at high risk for treatment related complications.

E-20. Women of childbearing potential (<2 years after last menstruation) not willing to use highly-effective means of contraception.

E-21. Pregnant or lactating women.

E-22. History of severe allergic, anaphylactic, or other hypersensitivity reactions to chimeric or humanized antibodies or fusion proteins.

E-23. Known hypersensitivity or allergy to biopharmaceuticals produced in Chinese hamster ovary cells or to any component of the atezolizumab formulation.

E-24. Known hypersensitivity reaction or allergy to drugs chemically related to carboplatin, paclitaxel, or their excipients that contraindicates the subject's participation.

STUDY ENDPOINTS

PRIMARY ENDPOINTS

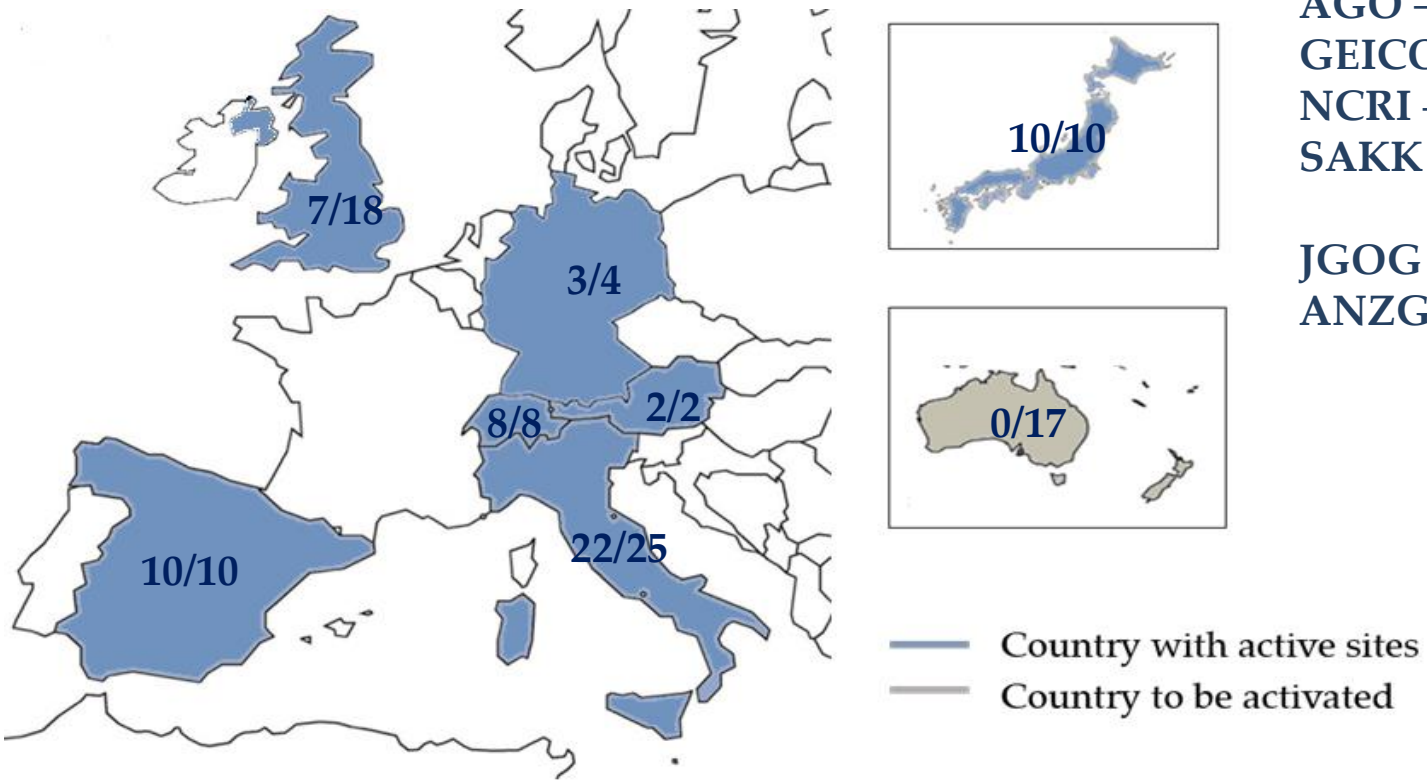
Overall survival and progression free survival (PFS)

SECONDARY ENDPOINTS

- PFS by micro satellite instability (MSI) status
- PFS2 by PD-L1 status
- Objective Response Rate
- Quality of life
- Safety

PARTICIPATING COUNTRIES/SITES

94 sites



National Groups:

MaNGO – Italy
A-AGO – Austria
AGO – Germany
GEICO – Spain
NCRI – UK
SAKK – Switzerland

JGOG – Japan
ANZGOG – Australia/New Zealand

ENROLLMENT AND UPDATE

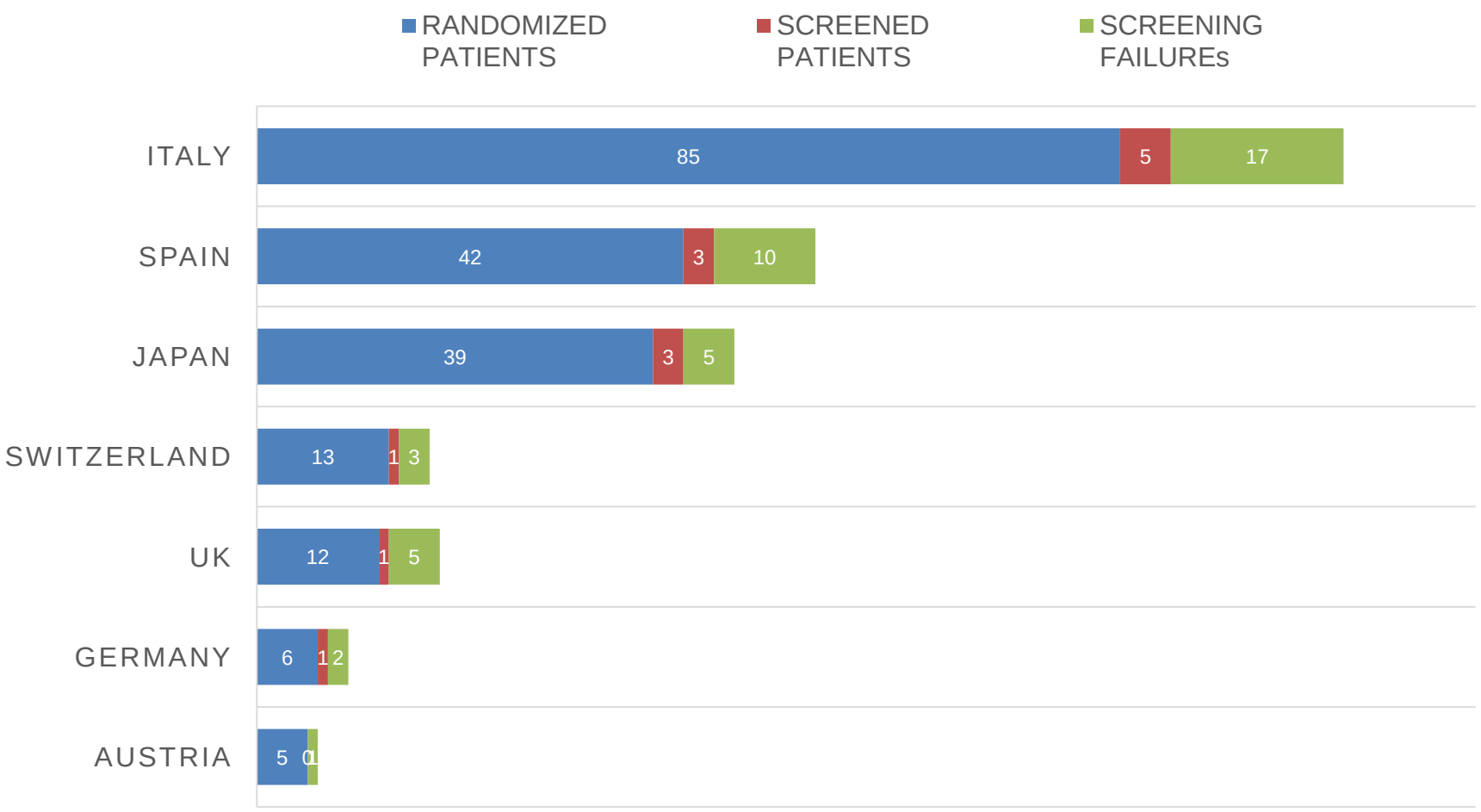
Study Duration

- Accrual: 2 years (Oct 2018 - Oct 2020)
- Follow-up: 2 years

Study update (25th June 2020)

- No. of randomized patients: 202
- No. of patients under screening: 14
- No. of screening failures: 43 (16.6%)

ENROLLMENT IN EACH COUNTRY



STUDY CONTACTS

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FOR DETAILS PLEASE SEE https://clinicaltrials.gov/ct2/show/NCT03603184